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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/637,190	08/11/00	HUNG M	12005-002001

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EXAMINER	
CANELLA,K	
ART UNIT	PAPER NUMBER
1642	4

DATE MAILED: 08/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/637,190	Hung et al
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-20* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-20* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *1*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Claims 1-20 are pending and examined on the merits.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 11-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining whether a subject with squamous cell carcinoma has lymph node metastasis comprising comparing the levels of maspin gene expression wherein a level of gene expression above a threshold level is indicative that the subject is free of metastatic cells in the lymph nodes, does not reasonably provide enablement for a method for determining whether a subject with squamous cell carcinoma has lymph node metastasis comprising comparing the levels of maspin gene expression wherein a level of gene expression below a threshold level is indicative that the subject is free of metastatic cells in the lymph nodes, or comparing the levels of maspin gene expression to determine if a patient has a lymph node containing cancerous cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Claim 11 is drawn to a level of maspin gene expression above a threshold being indicative of nodal cancer. Claim 16 is drawn to a level of maspin gene expression below a threshold level being indicative of a patient being free of nodal cancer. The specification teaches in Table I that no patients expressing high levels of maspin had nodal stage squamous cell carcinoma, although patients expressing intermediate to low levels of maspin represented subjects with and without nodal stage cancer, therefore only high levels of maspin expression can be correlated with the absence of nodal involvement as low and intermediate levels of maspin expression were found in both sets of patients. Further, the data presented in Table I

teaches against a methods wherein a level of maspin gene expression below a threshold level is indicative that the subject is free of metastatic cells in the lymph nodes, as low to intermediate levels of maspin gene expression were not correlated to the absence of nodal involvement (out of 29 patients having low to intermediate maspin gene expression, 10 had nodal stage cancer and 19 were free of nodal stage cancer). Therefore, levels below the "high" threshold were not predictive of lymph node metastasis.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 1-10 are rejected under 35 U.S.C. 102(a) as being anticipated by Xia et al (Oncogene, 2000, Vol. 19, pp. 2398-2403). Claims 1 and 6 are drawn to methods for determining the relative probability of survival comprising comparing the level of maspin gene expression with a threshold level, wherein a level above the threshold level indicates a relatively high probability of survival (claim 1) and a level below the threshold level indicates a relatively low probability of survival (claim 6). Claims 2, 3, 7 and 8 embody the measurement of the maspin gene product at the protein level. Claims 4, 5, 9 and 10 embody the measurement of the maspin gene product at the mRNA level. Xia et al teach that levels of maspin gene expression above a threshold level were associated with better rates of survival in patients having squamous cell carcinoma of the head and neck, and that conversely, levels of maspin gene expression below a threshold level were associated with low probabilities of survival in said patients. Xia et al teach the measurement of the maspin gene product at the protein level by the polyclonal antibody AbS4A, as well as measurement at the mRNA level in Northern Blot analysis (figure 3).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sager et al (USP 5,470,970) in view of Ding et al (Proceedings of the American Association of Cancer Research, 1996, Vol. 37, pp. A627) and either Gregory et al (USP 5,932,210) or Hung et al (USP 6,197,754). Claims 1 and 6 are drawn to methods for determining the relative probability of survival comprising comparing the level of maspin gene expression with a threshold level, wherein a level above the threshold level indicates a relatively high probability of survival (claim 1) and a level below the threshold level indicates a relatively low probability of survival (claim 6). Claims 2, 3, 7 and 8 embody the measurement of the maspin gene product at the protein level. Claims 4, 5, 9 and 10 embody the measurement of the maspin gene product at the mRNA level. Sager et al teach that maspin functions as a tumor suppressor gene in breast cancer. Sager et al teach the determination of maspin gene expression by either detection at the protein level by a polyclonal or monoclonal antibody, or by detection at the mRNA level. Ding et al teach that in addition to breast epithelial cells, maspin gene expression was also detected in squamous cell carcinomas of

the esophagus and tongue. Either Gregory et al (column 12, lines 64-67) or Hung et al teach that the presence of a tumor suppressor gene product (column 40, lines 11-14) is correlated with increased survival time. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to correlate relative survival times in patients suffering from squamous cell carcinomas with the expression of the maspin tumor suppressor by either measuring protein levels or mRNA levels of maspin. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Gregory or Hung on the increased survival times of patients expressing tumor suppressor genes and the teachings of Ding on the expression of the maspin gene product in squamous cell carcinomas of the esophagus and tongue.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
July 29, 2001

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